REMARKS

With entry of the current amendment, claim 22 has been amended and new claims 47 and 48 have been added. Claims 21-30 and 43-48 are therefore under examination.

Applicant notes that claims 1-17 were cancelled in Applicant's amendment dated October 30, 2003, not claims 1-18. Accordingly, 18-20 and 31-40 are properly withdrawn from consideration by the Examiner pursuant to the restriction requirement.

The amendments to the specification and claims add no new matter.

The amendment to the specification adds the ATCC deposit information for the hybridoma cell line for the antibody 2C1H7.

Claim 22 has been amended to recite a method of modifying a dose of a β-tubulin modifying agent that is administered to a patient. Support can be found, *e.g.,* in claim 22 as originally filed and in the application, *e.g.,* at page 2, line 32 bridging to page 3, line 6.

New claim 47 recites a monoclonal antibody that specifically binds to a peptide ATMSGVTTCLRFPGQLNA that comprises a modified cysteine residue. Support for the amendment can be found, *e.g.,* on page 20, starting at line 29 and bridging to page 30, line 6, which teaches the modified β2-tubulin peptide that was used to generate 2C1H7; and page 24, lines 3-11, which teach multiple monoclonal antibodies that specifically bind to the modified β-tubulin peptide.

New claim 48 recites that the monoclonal antibody is 2C1H7 (ATCC Accession Number PTA-2686). Support can be found, *e.g.,* in original claim 27.

The comments/rejection are addressed in the order set forth in the Office Action mailed November 12, 2004.

Rejection under 35 U.S.C. § 112, first paragraph

Claim 27 was rejected as lacking adequate written description support. The Examiner notes that the specification lacks complete deposit information for the recited hybridoma cell lines. Applicant has amended the specification to provide the ATCC deposit information where available. Applicant respectfully requests that this rejection be held in

abeyance. Upon identification of allowable claims, the claims will be amended to recite the deposit information, or alternatively, subject matter relating to the hybridomas that have not been deposited will be cancelled.

Rejections under 35 U.S.C. § 112, second paragraph

Claims 22 and 27 were rejected as indefinite.

Claim 22 was allegedly indefinite as lacking proper antecedent basis for "the dose of the β-tubulin..." and as not clearly setting forth a method that is commensurate with the endpoint recited in independent claim 21, from which it depends. Although Applicant disagrees, in order to expedite prosecution, claim 22 has been amended to address both issues. Applicant believes that these amendments overcome the rejections and therefore requests their withdrawal.

Claim 27 was rejected as allegedly indefinite in the recitation of the various designations of the monoclonal antibodies. As noted above, upon identification of allowable claims, the claims will be amended to recite appropriate deposit information, or alternatively, subject matter relating to the hybridomas that have not been deposited will be cancelled. Applicant therefore respectfully requests that this rejection be held in abeyance.

Rejection under 35 U.S.C. § 103

Claims 21-30 and 43-46 were rejected as allegedly obvious over Shan *et al.* (*Proc. Natl. Acad. Sci. USA* 96:5686-5691, 1999) in combination with various secondary references. The rejection describes Shan *et al.* as teaching a method of monitoring the amount of modified β-tubulin isotype in a sample treated with a synthetic compound that modifies Cys-239 of β2- and β4-tubulin isotypes. The method employs anti-β tubulin antibodies. The Examiner argues that it is reasonable to conclude that the antibodies of Shan *et al.* are the same as the β-tubulin antibodies employed in the instant invention because they allegedly possess the same binding affinity to Cys-239 of β2 and β4 isotypes. She therefore concludes that the claimed methods are unpatentable over Shan *et al.* and the secondary references (that teach monitoring patient samples, use of standard curve and adjustment of dosages of agents administered to

patients, and an antibody that is covalently linked to a detectable label). Applicant respectfully traverses this rejection.

As the Examiner knows, in order to establish a *prima facie* case of obviousness, the rejection must demonstrate that: (1) there is some suggestion or motivation to modify the reference or combine the reference teachings; (2) there is a reasonable expectation of success: and (3) the prior art references suggest all the claim elements. *See, e.g.*, MPEP § 2143; *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). Further, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. (*see, In re Vaeck, supra*). The argument advanced by the Examiner fails in all of these aspects.

The Examiner contends that it is reasonable to conclude that the antibodies of Shan *et al.* are the same as the β-tubulin antibodies employed in the instant invention. However, contrary to the Examiner's position, the cited passages do not provide proper support for this assertion. The Figure legend to Figure 1 indicates only that anti-β-tubulin antibodies were used in an immunoblotting experiment. In the section "T138067 Modified...." on page 5688, column 2, it is explained that the various β-tubulin isotypes were detected with isotype-specific antibodies. The section "T138067 Binds to Cys 239..." adds nothing regarding the binding specificity of the antibodies. Thus, although the antibodies are able to detect β-tubulin labeled with tritiated T138067, there is no evidence that they specifically bind to modified β-tubulin, and not unmodified β-tubulin.

The initial burden is on the examiner to provide some suggestion of the desirability of doing what the inventor has done (MPEP § 2142). Here, the Examiner fails to meet this burden. The blind assertion that one of skill could reasonably predict that the antibodies of Shan *et al.* would in fact specifically bind to modified β-tubulin is insufficient. "To support the conclusion that the claimed invention is directed to obvious subject matter, either the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." (MPEP § 2142,

quoting *Ex parte Clapp*, 227 USPQ972, 973 (Bd. Pat. App. & Inter. 1985). As explained above, the references do not expressly suggest or imply the claimed subject matter.

Further, the Examiner's arguments provide no motivation from the art as to why the mere fact that isotype-specific antibodies bind to β-tubulin labeled with tritiated T138067 would lead the artisan to select those antibodies for use in a method of monitoring the amount of modified β-tubulin using an antibody that specifically binds to modified β-tubulin. Moreover, assuming *arguendo* that one of skill had a motivation to try the antibodies of Shan *et al.* in the methods of the invention, the Examiner provides no convincing line of reasoning that they would reasonably be expected to work in the manner set forth in the claims.

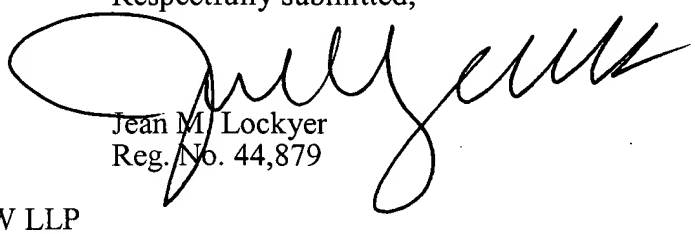
The secondary references cited in the rejection provide nothing to overcome the deficiencies of Shan *et al.* and nothing more to support the Examiner's reasoning. In view of the foregoing, the Examiner fails to establish a proper case of *prima facie* obviousness. Applicant therefore request withdrawal of the rejection.

CONCLUSION

Applicant believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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